

Claims

- 1) A method of assessing cardiac neurotransmission in a human subject comprising:
- 5 vi) administration to said subject of an amount suitable for *in vivo* imaging of an adrenergic imaging agent;
- vii) *in vivo* imaging of said subject using said adrenergic imaging agent;
- viii) administration of an adrenergic interfering agent to said subject;
- ix) repeating steps (i) and (ii); and,
- 10 x) comparing the images obtained in steps (ii) and (iv).
- 2) The method of claim 1 wherein said cardiac neurotransmission is assessed to investigate the status of a cardioneuropathy in said human subject.
- 3) The method of claim 2 wherein said cardioneuropathy is a primary
- 15 cardioneuropathy related to:
- (i) a dysautonomia;
- (ii) heart transplantation; or,
- (iii) idiopathic ventricular tachycardia and fibrillation.
- 4) The method of claim 2 wherein said cardioneuropathy is a secondary
- 20 cardioneuropathy related to:
- (i) dilated cardiomyopathy;
- (ii) coronary artery disease;
- (iii) hypertrophic cardiomyopathy;

- (iv) arrhythmogenic right ventricular cardiomyopathy;
 - (v) diabetes mellitus;
 - (vi) hypertension; or,
 - (vii) drug-induced cardiotoxicity.
- 5 5) The method of claim 1 wherein said adrenergic interfering agent is selected from:
- (i) tricyclic antidepressants;
 - (ii) beta blockers;
 - (iii) calcium channel blockers;
 - 10 (iv) sympathomimetic agents; and,
 - (v) cocaine.
- 6) The method of claim 5 wherein said adrenergic interfering agent is a tricyclic antidepressant selected from desipramine, amitriptyline and imipramine.
- 15 7) The method of claim 6 wherein said adrenergic interfering agent is amitriptyline.
- 8) The method of claim 1 wherein said adrenergic imaging agent is selected from labelled forms of *m*IBG, *m*FBG, hydroxyephedrine, ephedrine, fluorodopamine, CGP, carazolol and MQNB.
- 20 9) The method of claim 8 wherein said adrenergic imaging agent is radioiodinated *m*IBG.
- 10) The method of claim 9 wherein said adrenergic imaging agent is ¹²³I *m*IBG.

11)The method of claim 1 wherein said *in vivo* imaging is external imaging carried out by SPECT or PET.

12)The method of claim 11 wherein said external imaging is carried out by SPECT.

5 13)A method of assessing cardiac neurotransmission in a human subject comprising:

- i) administration of a non-therapeutic dose of an adrenergic interfering agent to said subject;
- 10 ii) administration to said subject of an amount suitable for *in vivo* imaging of an adrenergic imaging agent; and,
- iii) *in vivo* imaging of said subject.

14)The method of claim 13 wherein said cardiac neurotransmission is assessed to investigate the status of a cardioneuropathy in said human subject.

15 15)The method of claim 14 wherein said cardioneuropathy is a primary cardioneuropathy related to:

- (i) a dysautonomia;
- (ii) heart transplantation; or,
- (iii) idiopathic ventricular tachycardia and fibrillation.

20 16)The method of claim 14 wherein said cardioneuropathy is a secondary cardioneuropathy related to:

- (i) dilated cardiomyopathy;
- (ii) coronary artery disease;
- (iii) hypertrophic cardiomyopathy;

- (iv) arrhythmogenic right ventricular cardiomyopathy;
- (v) diabetes mellitus;
- (vi) hypertension; or,
- (vii) drug-induced cardiotoxicity.

5 17)The method of claim 13 wherein said adrenergic interfering agent is selected from:

- (i) tricyclic antidepressants;
- (ii) beta blockers;
- (iii) calcium channel blockers;
- 10 (iv) sympathomimetic agents; and,
- (v) cocaine.

18)The method if claim 17 wherein said adrenergic interfering agent is a tricyclic antidepressant selected from desipramine, amitryptaline and imipramine.

15 19)The method of claim 18 wherein said adrenergic interfering agent is amitryptaline and the non-therapeutic dose is between 10 and 50mg.

20)The method of claim 13 wherein said adrenergic imaging agent is selected from labelled forms of *m*IBG, *m*FBG, hydroxyephedrine, ephedrine, fluorodopamine, CGP, carazolol and MQNB.

20 21)The method of claim 20 wherein said adrenergic imaging agent is radioiodinated *m*IBG.

22)The method of claim 21 wherein said adrenergic imaging agent is ¹²³I *m*IBG.

23)The method of claim 13 wherein said *in vivo* imaging is external imaging carried out by SPECT or PET.

24)The method of claim 23 wherein said external imaging is carried out by SPECT.

5 25)A method of determining the viability of a region of adrenergically innervated tissue in a human subject, comprising:

- (v) performing *in vivo* imaging of said subject using an adrenergic imaging agent;
- 10 (vi) administration to said subject of an adrenergic interfering agent;
- (vii) repeating step (i); and,
- (viii) comparing the images obtained in steps (i) and (iii).

26)The method of claim 25 wherein said adrenergically innervated tissue is the myocardium.

15 27)The method of claim 25 wherein said viability of a region of adrenergically innervated tissue is assessed to investigate the status of a cardioneuropathy in said human subject.

28)The method of claim 27 wherein said cardioneuropathy is a primary cardioneuropathy related to:

- 20 (i) a dysautonomia;
- (ii) heart transplantation; or,
- (iii) idiopathic ventricular tachycardia and fibrillation.

29)The method of claim 27 wherein said cardioneuropathy is a secondary cardioneuropathy related to:

- 5
- (i) dilated cardiomyopathy;
 - (ii) coronary artery disease;
 - (iii) hypertrophic cardiomyopathy;
 - (iv) arrhythmogenic right ventricular cardiomyopathy;
 - (v) diabetes mellitus;
 - (vi) hypertension; or,
 - (vii) drug-induced cardiotoxicity.

30) The method of claim 25 wherein said adrenergic interfering agent is selected from:

- 10
- (i) tricyclic antidepressants;
 - (ii) beta blockers;
 - (iii) calcium channel blockers;
 - (iv) sympathomimetic agents; and,
 - (v) cocaine.

15 31) The method of claim 30 wherein said adrenergic interfering agent is a tricyclic antidepressant selected from desipramine, amitriptyline and imipramine.

32) The method of claim 31 wherein said adrenergic interfering agent is amitriptyline.

20 33) The method of claim 25 wherein said adrenergic imaging agent is selected from labelled forms of *m*IBG, *m*FBG, hydroxyephedrine, ephedrine, fluorodopamine, CGP, carazolol and MQNB.

- 34)The method of claim 33 wherein said adrenergic imaging agent is radioiodinated *m*IBG.
- 35)The method of claim 34 wherein said adrenergic imaging agent is ¹²³I *m*IBG.
- 5 36)The method of claim 25 wherein said *in vivo* imaging is external imaging carried out by SPECT or PET.
- 37)The method of claim 36 wherein said external imaging is carried out by SPECT.
- 10 38)A method of imaging the sympathetic innervation of a tissue of a human subject comprising:
- (v) *in vivo* imaging with an adrenergic imaging agent;
 - (vi) administration of an adrenergic interfering agent;
 - (vii) repeating step (i); and,
 - (viii) comparing the images obtained in steps (i) and (iii).
- 15 39)The method of claim 38 wherein said tissue is the myocardium.
- 40)The method of claim 38 wherein said sympathetic innervation is imaged to investigate the status of a cardioneuropathy in said human subject.
- 20 41)The method of claim 40 wherein said cardioneuropathy is a primary cardioneuropathy related to:
- (i) a dysautonomia;
 - (ii) heart transplantation; or,
 - (iii) idiopathic ventricular tachycardia and fibrillation.

42)The method of claim 40 wherein said cardioneuropathy is a secondary cardioneuropathy related to:

- (i) dilated cardiomyopathy;
- (ii) coronary artery disease;
- 5 (iii) hypertrophic cardiomyopathy;
- (iv) arrhythmogenic right ventricular cardiomyopathy;
- (v) diabetes mellitus;
- (vi) hypertension; or,
- (vii) drug-induced cardiotoxicity.

10 43)The method of claim 38 wherein said adrenergic interfering agent is selected from:

- (i) tricyclic antidepressants;
- (ii) beta blockers;
- (iii) calcium channel blockers;
- 15 (iv) sympathomimetic agents; and,
- (v) cocaine.

44)The method of claim 43 wherein said adrenergic interfering agent is a tricyclic antidepressant selected from desipramine, amitriptyline and imipramine.

20 45)The method of claim 44 wherein said adrenergic interfering agent is amitriptyline.

- 46)The method of claim 45 wherein said adrenergic imaging agent is selected from labelled forms of *m*IBG, *m*FBG, hydroxyephedrine, ephedrine, fluorodopamine, CGP, carazolol and MQNB.
- 5 47)The method of claim 38 wherein said adrenergic imaging agent is radioiodinated *m*IBG.
- 48)The method of claim 47 wherein said adrenergic imaging agent is ¹²³I *m*IBG.
- 49)The method of claim 38 wherein said *in vivo* imaging is external imaging carried out by SPECT or PET.
- 10 50)The method of claim 49 wherein said external imaging is carried out by SPECT.
- 51)A method of operating an external imaging apparatus using signal data derived from an adrenergic imaging agent previously administered to a human subject, said method being carried out both before and after the previous administration of an adrenergic interfering agent to said subject and then comparing the signal data so derived.
- 15 52)The method of claim 51 wherein said adrenergic interfering agent is selected from:
- (i) tricyclic antidepressants;
 - 20 (ii) beta blockers;
 - (iii) calcium channel blockers;
 - (iv) sympathomimetic agents; and,
 - (v) cocaine.

- 53)The method of claim 52 wherein said adrenergic interfering agent is a tricyclic antidepressant selected from desipramine, amitryptaline and imipramine.
- 54)The method of claim 53 wherein said adrenergic interfering agent is
5 amitryptaline.
- 55)The method of claim 51 wherein said adrenergic imaging agent is selected from labelled forms of *m*IBG, *m*FBG, hydroxyephedrine, ephedrine, fluorodopamine, CGP, carazolol and MQNB.
- 56)The method of claim 55 wherein said adrenergic imaging agent is
10 radioiodinated *m*IBG.
- 57)The method of claim 56 wherein said adrenergic imaging agent is ¹²³I *m*IBG.
- 58)The method of claim 51 wherein said external imaging apparatus is a SPECT or PET apparatus.
- 59)The method of claim 58 wherein said external imaging apparatus is a
15 SPECT apparatus.
- 60)Use of an adrenergic imaging agent in the manufacture of a medicament for use in *in vivo* imaging of the sympathetic innervation of a human subject wherein said *in vivo* imaging is carried out both before
20 and after the administration of an adrenergic interfering agent and comparing the images so obtained.
- 61)The use of claim 60 wherein said sympathetic innervation is in the myocardium of said subject.
- 62)The use of claim 60 wherein said sympathetic innervation is imaged to
25 investigate the status of a cardioneuropathy in said human subject.

63)The use of claim 62 wherein said cardioneuropathy is a primary cardioneuropathy related to:

- (i) a dysautonomia;
- (ii) heart transplantation; or,
- 5 (iii) idiopathic ventricular tachycardia and fibrillation.

64)The use of claim 62 wherein said cardioneuropathy is a secondary cardioneuropathy related to:

- (i) dilated cardiomyopathy;
- (ii) coronary artery disease;
- 10 (iii) hypertrophic cardiomyopathy;
- (iv) arrhythmogenic right ventricular cardiomyopathy;
- (v) diabetes mellitus;
- (vi) hypertension; or,
- (vii) drug-induced cardiotoxicity.

15 65)The use of claim 60 wherein said adrenergic interfering agent is selected from:

- (i) tricyclic antidepressants;
- (ii) beta blockers;
- (iii) calcium channel blockers;
- 20 (iv) sympathomimetic agents; and,
- (v) cocaine.

66)The use of claim 65 wherein said adrenergic interfering agent is a tricyclic antidepressant selected from desipramine, amitryptaline and imipramine.

5 67)The use of claim 66 wherein said adrenergic interfering agent is amitryptaline.

68)The use of claim 60 wherein said adrenergic imaging agent is selected from labelled forms of *m*IBG, *m*FBG, hydroxyephedrine, ephedrine, fluorodopamine, CGP, carazolol and MQNB.

10 69)The use of claim 68 wherein said adrenergic imaging agent is radioiodinated *m*IBG.

70)The use of claim 69 wherein said adrenergic imaging agent is ¹²³I *m*IBG.

71)The use of claim 60 wherein said *in vivo* imaging is external imaging carried out by SPECT or PET.

15 72)The use of claim 71 wherein said external imaging is carried out by SPECT.

73)A kit for use in the method of claim 1 which comprises:

- 20
- (i) an adrenergic interfering agent; and,
 - (ii) an adrenergic imaging agent in a form suitable for carrying out said *in vivo* imaging steps, or a precursor thereof.

74)The kit of claim 73 wherein said adrenergic interfering agent is selected from:

- 25
- (i) tricyclic antidepressants;
 - (ii) beta blockers;

- (iii) calcium channel blockers;
- (iv) sympathomimetic agents; and,
- (v) cocaine.

5 75)The kit of claim 74 wherein said adrenergic interfering agent is a tricyclic antidepressant selected from desipramine, amitryptaline and imipramine.

76)The kit of claim 75 wherein said adrenergic interfering agent is amitryptaline.

10 77)The kit of claim 73 wherein said adrenergic imaging agent is selected from labelled forms of *m*IBG, *m*FBG, hydroxyephedrine, ephedrine, fluorodopamine, CGP, carazolol and MQNB.

78)The kit of claim 77 wherein said adrenergic imaging agent is radioiodinated *m*IBG.

79)The kit of claim 78 wherein said adrenergic imaging agent is ¹²³I *m*IBG.